be extended intravascular from the catheter tip laterally into periadventitial vascular tissue with was analyzed. Systemic application (2.5 mgxkg^{-1}) and LDD (PFII, 5 mg) was performed in femoral and carotid arteries of 16 pigs after standardized vessel injury with a atherectomy device. The vessels were excised between 15 minutes and 21 days after PF II injection and fixed in liquid N_2 for semiquantitative fluorescent microscopy with a reference signal. Systemic application: Intima showed a threefold higher fluorescence compared to other vessel wall layers with a maximum in all layers at 24 hours (media 50%, adventitia 85%). Maximum fluorescence (100%) was found 24 hours after injection. LDD: 95% of the applications were successful and led to a maximum fluorescence in periadventitial layers after 30 minutes (300% intima, 150% media, 380% periadventitial layer). Even after 21 days a significant PF II related fluorescence was detectable in periadventitial tissue (38%).

LDD achieves a 380% higher drug content than high dose systemic application. This is the first catheter system that enables a LDD over 21 days by periadventitial depots.

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984-27 Arterial Remodeling Contributes to Restenosis After Angioplasty, but is Prevented by Stenting in the Atherosclerotic Micropig

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We previously showed that 50% of angiographic late lumen loss (LL) following balloon dilation (PTA) was due to remodeling (REM) of the artery. By scaffolding the artery, the stent is likely to prevent remodeling. To test this hypothesis, we compared PTA and stenting of peripheral arteries of Yucatan micropigs in a combined denudation and diet-induced atherosclerosis model. Angiograms were taken before, during and after angioplasty and at termination (42 days after intervention). Acute gain (AG) and LL were quantitatively measured with digital calipers. Intravascular ultrasound (IVUS) was performed in 5 stented arteries. The peripheral arterial tree was pressure perfusion fixed, processed for histology and morphometrically analyzed with a computer-based system. Intimal Hyperplasia (IH) and Media (M) were expressed as mean Thickness (IHT, MT) for comparison with angiography. *Results:*

	n	AG(mm)	LL(mm)	2xIHT(mm)	MT(mm)	REM%
control	12	-	0.14 ± 0.11	0.07 ± 0.02	0.14 ± 0.02	0
PTA	12	0.35 ± 0.06	0.27 ± 0.08	0.14 ± 0.03	0.15 ± 0.04	48 ± 12*
stent	10	0.42 ± 0.10	0.51 ± 0.07	0.47 ± 0.08†	0.14 ± 0.02	6 ± 12

mean ± sem, *$p < 0.05$ compared to zero, †$p < 0.01$ stent versus PTA

In 5 stented arteries, IH measured with IVUS and histology was 4.93 ± 0.91 and 4.41 ± 1.25 mm^2, respectively. The correlation coefficient was 0.89, $p = 0.045$.

We conclude that after the stent prevents remodeling, i.e. shrinkage after angioplasty. In stented arteries, restenosis is entirely due to intimal hyperplasia which is significantly larger than after balloon dilation alone. Stented arteries may therefore preferentially benefit from antiproliferative agents, whereas adjunctive therapy with balloon angioplasty should also be aimed at reducing remodeling.

984-28 Vitamin E does not Improve Regenerated Endothelium Dysfunction Following Balloon-induced Vascular Injury

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Fibromuscular intimal injury is frequent after coronary angioplasty. Peroxidation of circulating and membrane lipids have been implicated in intimal hyperplasia and endothelial dysfunction following arterial trauma. The aim of this study was to evaluate the effects of the natural membrane antioxidant vitamin E on the regenerated endothelium dysfunction. A first group of rats (n = 10) was pretreated with vitamin E (VE) 100 IU/kg/day for a week before undergoing aortic (thoracic) endothelial denudation with a Fogarty catheter. Rats were then fed with the same VE supplemented diet for a period of 2 months. A second group (n = 10) was similarly denuded and fed with soya oil (SO), VE vehicle, for the same period. A third group (n = 10) was denuded (DN) without any treatment and a fourth group was used as control (CL) without denudation. Endothelial-dependent and independent relaxation were assessed in organ chambers with acetylcholine (ACH 10^{-9}–10^{-4} mol/L) and sodium nitroprusside (SNP 10^{-9}–10^{-4} mol/L) respectively. Endothelial regeneratin was evaluated with Evan's blue staining. Vascular relaxation to SNP was not affected either by the regeneration process or the VE supplementation. However, endothelial-dependent relaxation to ACH was significantly impeded in the regenerated endothelium compared to control ($p < 0.01$) and was not influenced by the VE or the SO (p = NS) [ED_{50} (−logM); CL:6.8 ± 0.1, DN:6.3 ± 0.1, VE:6.0 ± 0.2, SO: 6.1 ± 0.1, ANOVA]. Morphometric studies with Evan's blue staining showed over 95% regeneration of the endothelial surface of the denuded aortas. Our present results suggest that in spite of a complete anatomical regeneration, endothelial cells do not resume predenudation function. Endothelial-independent relaxation was preserved in all groups indicating that smooth muscle function was not altered by the regenerating process. The presence of dietary supplement of VE (up to 20-fold the dietary requirement) did not improve the endothelial dysfunction in the endothelium-regenerated rat aorta model.

984-29 Modulation of s-Homocysteine Associated with Intimal Thickening After Balloon Angioplasty Injury of the Rabbit Iliac Artery

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Hyperhomocysteinemia is associated with arterial disease. Elevated levels of s-homocystein (Hcy) have been suggested to cause intimal injury and smooth muscle cell recruitment. Since a similar vessel wall response is also seen in restenotic lesions after balloon angioplasty, we studied the effects of moderate reduction and elevation of s-Hcy levels on the potentiation of arterial wall thickening after balloon injury in the iliac artery of rabbits.

Methods: 16 female Chinchilla (Chbb:CH) rabbits were randomized to receive either Hcy-lowering therapy with pryridoxin, cobalamin, folic acid and Betain (group 1, weight 3.9 kg) or Hcy-increasing therapy with methionin (group 2, weight 3.8 kg, p = NS). After one week transcatheter balloon angioplasty was performed via right carotidotomy using an oversized (3.0 mm) balloon catheter. Angiography was performed after angioplasty and after 9 weeks, when the rabbits were sacrified and perfusion-fixed. Injury response was measured by histomorphometry.

Results: Pre-treatment s-Hcy-levels were 17.2 + 6.9 vs 16.7 + 5.3 mmol/l for group 1 and 2 (p = NS), at the time of angioplasty 13.5 + 2.9 vs 20.0 + 7.0 ($p < 0.05$) and these differences remained throughout the study. Histomorphometry showed intima/media area ratio 0.44 + 0.17 vs 0.73 + 0.24 ($p = 0.03$), intima/media thickness ratio 1.11 + 0.93 vs 2.00 + 2.79 ($p = 0.03$) and absolute intima thickness 0.11 + 0.01 vs 0.22 ± 0.04 mm ($p = 0.03$) for group 1 and 2 resp. Angiographic videodensitometry was consistent with the histomorphometric findings.

Conclusion: Hyperhomocysteinemia contributes to intimal thickening in the rabbit iliac artery after balloon angioplasty injury.

984-30 Use of Electroporated Platelets as a Novel Drug Delivery System in Preventing Complications of Coronary Angioplasty

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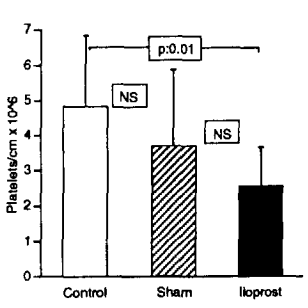
Acute occlusion and more importantly late restenosis remain important limitations of various percutaneous intervention techniques. Local delivery of agents is a theoretically appealing method of preventing these complications. Due to their affinity for areas of arterial injury, platelets may serve as an ideal delivery vehicle. Compounds can be entrapped within platelets during exposure of the cells to a sequence of high voltage discharges. This process, termed electroporation, occurs via simple diffusion through field induced membrane pores. We studied the prostacyclin analogue, Iloprost, to test the potential of this system. We evaluated the extent of platelet deposition at the site of balloon-mediated vascular injury in normal rabbit femoral arteries. Arterial injury was performed to the femoral arteries bilaterally using a 2.5 mm balloon in 12 NZW rabbits. Either normal (control), electroporated without Iloprost (sham), or electroporated with Iloprost (Iloprost) donor platelets (5×10^8) were infused at the time of the balloon injury. Platelets were electroporated with 5 cycles of high voltage discharges in a high potassium medium,



and resealed by incubation at 37°C for 40 min. For Iloprost loading, Iloprost at a concentration 20 μg/ml was added to the medium. Quantification of platelet deposition at the site of arterial injury was obtained using indium-111 labeled platelets infused 1/2 hour prior to balloon injury. Involved arterial segments were excised 2 hours after arterial injury. The results are expressed as platelets per centimeter of artery (graph). Further, preliminary results in an atherosclerotic rabbit model demonstrated a 64% reduction in platelet deposition using iloprost loaded platelets.

Conclusion: Taking advantage of a natural physiologic process after arterial injury, this delivery system offers a unique "piggy-back" mechanism of drug delivery. Platelet encapsulation with Iloprost and other agents deserves further study.

985 Pediatric Cardiac Surgery/Postoperative

Wednesday, March 22, 1995, 9:00 a.m.–11:00 a.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: 10:00 a.m.–11:00 a.m.

985-54 Do Central Pulmonary Arteries Grow Following Bidirectional Superior Cavopulmonary Anastomosis?

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The role of bidirectional superior cavopulmonary anastomosis (BCPA) in palliation of complex congenital heart defects is now established but little is known about the growth of pulmonary arteries following this operation.

Between 1987 and 1993, 74 children underwent BCPA in 2 centres. Of these 21 were further studied by postoperative angiography and are the subject of this investigation. Their median age at BCPA was 23 months (range 1–108 months). BCPA was undertaken through a thoracotomy in 5 and through a midline sternotomy on cardiopulmonary bypass in 16. Competitive sources of pulmonary blood flow were left open in 9 patients. Follow-up angiograms were performed 1–65 months (median 11 months) postoperatively. Z-scores, which standardize pulmonary arteries to body surface area, were calculated from measurement of the diameter immediately prior to the first branching point of each pulmonary artery.

The pre- and postoperative body surface areas increased from 0.46 m^2 (SD 0.21) to 0.66 m^2 (SD 0.22). The pre- and postoperative Z-scores of the right pulmonary artery were −1.77 (SD 2.63) and −0.38 (SD 1.69) respectively. The left pulmonary artery Z-scores were −0.08 (SD 2.14) and −0.17 (SD 1.31) pre- and post- operatively. In the subset of 13 patients with reduced pulmonary blood flow (O_2 saturation <0.75) preoperatively, the right pulmonary artery grew in excess of somatic growth (mean Z-score −2.63 pre and −0.62 post-operatively; $p = 0.003$). There was no difference in growth of the pulmonary arteries in patients with and without competitive pulmonary blood flow.

Our preliminary results demonstrate that adequate growth of the pulmonary arteries occurs following BCPA in short term follow-up.

985-55 Surgical Repair of Double Outlet Right Ventricle with Non-committed Ventricular Septal Defect

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Between January 1978 and June 1993, 32 patients presented for management of double outlet RV with non-committed VSD. 29 patients had definitive palliation or repair with 3 early and 1 late deaths (hospital mortality: 10.4%).

The VSD type was muscular in 4, inlet in 12 and perimembranous but distant from both great arteries in 16 patients. Complicating anomalies with a major influence on management were present in 23 children (72%). These included aortic arch interruption (3), coarctation of the aorta (4), pulmonary stenosis (11), pulmonary atresia (2), multiple VSDs (3), AV discordance (2), left atrial isomerism (3), unbalanced ventricles (8) and criss-cross AV connection (2) with 11 children having more than one of these lesions.

Initial palliation was performed in 20 patients and consisted of pulmonary artery banding in 8 (with repair of an interrupted aortic arch in 2), systemic-pulmonary artery shunt in 9 and repair of coarctation of the aorta in 3. Of these, 17 subsequently had definitive surgery: Fontan procedure in 9 and biventricular repair in 8 (arterial switch in one, intraventricular baffle in 7). 3 patients died following attempted biventricular repair. 12 patients underwent repair as the initial procedure: Fontan procedure in 2 and biventricular repair in 10 (arterial switch in 3 and intraventricular baffle in 7) with no deaths. Thus, of the 29 patients who had definitive surgery, 11 had Fontan procedures and 18 biventricular repair with no death in the Fontan group and 3 early deaths in the biventricular repair group (not statistically significant by Fischer's exact test, $p = 0.27$). Only 2 patients have required reoperations, both for residual VSDs. 9 of the Fontan procedures were undertaken in patients who had complex anatomy (e.g. AV discordance, unbalanced ventricles, multiple VSDs, atrial isomerism or pulmonary atresia), whereas 14 children of the biventricular repair group had non-complex anatomy ($p < 0.005$).

Surgery for double outlet RV with non-committed VSD needs to be tailored to individual patients, but biventricular repair was achieved in a substantial majority of patients with non-complex anatomy with relatively low risk and a low incidence of reoperations.

985-62 Outcome of Anomalous Origin of the Left Coronary Artery

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The outcome after surgical repair of anomalous origin of the left coronary artery from the pulmonary trunk (ALCAPA) remains incompletely defined, and transplantation has been advocated for patients with severe left ventricular dysfunction. We reviewed our institutional experience with ALCAPA since 1977 in 38 patients whose repair established a dual coronary circulation (7 early cases with LCA ligation were excluded) to assess whether cardiac function predicts outcome, the use of left ventricular assist device (LVAD), and postoperative complications of the current operative techniques. Surgical techniques included direct coronary reimplantation to the aorta in 11 pts, intrapulmonary baffling (Takeuchi) when the LCA could not reach the aorta directly in 25 pts, and modified Takeuchi in which an extrapulmonary baffle was fashioned from anterior and posterior walls of the pulmonary artery in 2 pts. The operative survival was 91%, 88%, and 100%, respectively (89% overall). All pts who died were <1yr old (3/19 Takeuchi, 1/10 reimplantation). Since its introduction at our institution in 1990, LVAD has been used in 4/16 pts, 1 Takeuchi pt who died and 3 reimplantation pts who all survived. Survival in pts <1 yr old was not different in those with severe dysfunction (shortening fraction (SF) <15%, 18/20) compared with moderate dysfunction (SF 16–25%, 4/5). Function returned to normal in all pts for whom followup is known past one year, regardless of the severity of preoperative dysfunction. Postoperative complications for Takeuchi pts included baffle leaks in 6/21 pts who underwent postoperative echocardiogram, supravalvar pulmonary stenosis in 13/20 pts for whom followup is known (<25 mmHg in 9 pts, 26–50 mmHg in 2 pts, >50 mmHg in 2 pts requiring reoperation), and progressive aortic regurgitation requiring aortic valve replacement in 1 pt. There were no complications in the two modified Takeuchi pts (6 and 12 mos followup) or in reimplantation pts.

Conclusions: (1) The degree of LV dysfunction at presentation does not predict survival in pts <1yr old, (2) current operative survival for ALCAPA does not justify consideration of transplantation, (3) LVAD may improve survival for some patients and should be available for postoperative management, and (4) supravalvar pulmonary stenosis occurs in a majority of Takeuchi pts, some of whom require reoperation; a modified technique may improve this postoperative complication rate.

985-63 Results of Norwood Operation for Lesions other than Hypoplastic Left Heart Syndrome

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Norwood's operation provides satisfactory palliation for neonates with hypoplastic left heart syndrome. The dominant physiologic features of hypoplastic left heart syndrome, ductal dependency of the systemic circulation and parallel pulmonary and systemic circulations, are shared by a multitude of other less common congenital heart malformations. Theoretically, these should be equally amenable to palliation by Norwood's operation. Since January 1990, 60 neonates with malformations other than hypoplastic left heart syndrome have undergone initial surgical palliation by Norwood's procedure. Diagnoses include single left ventricle with l-transposition of the great arteries (12), critical aortic stenosis (8), complex double outlet right ventricle (8), interrupted aortic arch with ventricular septal defect and subaortic stenosis (7), ventricular septal defect, subaortic stenosis, and coarctation of the aorta (7), aortic atresia with large ventricular septal defect (6), tricuspid atresia with transposition of the great arteries (6), heterotaxy syndrome with subaortic obstruction (3), and other (3). There were 10 hospital deaths and 50 survivors (83% survival). After the introduction of inspired carbon dioxide into the postoperative management protocol (1991), 42 of 47 patients survived (89% survival). Mortality is independent of diagnosis, and essentially the same as for hypoplastic left heart syndrome. With minor technical modifications, Norwood's operation provides satisfactory initial palliation for a wide variety of malformations characterized by ductal dependency of the systemic circulation, in anticipation of either a Fontan procedure or a biventricular repair.